

Amendments to the Specification:

Please amend the paragraph starting on page 3, line 1 as follows:

-- Currently two different predictive tools for MARs are available via the Internet. The ~~first~~ first one, MAR-Finder (~~<http://futuresoft.org/MarFinder>~~; Singh GB, Kramer JA and Krawetz SA, "Mathematical model to predict regions of chromatin attachment to the nuclear matrix", Nucleic Acid Research, 25:1419-1425, 1997) is based on set of patterns identified within several MARs and a statistical analysis of the co-occurrence of these patterns. MAR-Finder predictions are dependent of the sequence context, meaning that predicted MARs depend on the context of the submitted sequence. The other predictive software, SMARTest (~~<http://www.genomatix.de>~~; Frisch M, Frech K, Klingenhoff A, Cartharius K, Liebich I and Werner T, "In silico prediction of scaffold/matrix attachment regions in large genomic sequences", Genome Research, 12:349-354, 2001), use weight-matrices derived from experimentally identified MARs. SMARTest is said to be suitable to perform large-scale analyses. But actually aside its relative poor specificity, the amount of hypothetical MARs rapidly gets huge when doing large scale analyses with it, and in having no way to increase its specificity to restrain the number of hypothetical MARs, SMARTest becomes almost useless to screen for potent MARs from large DNA sequences. --

Please amend the paragraph starting on page 12, line 1 as follows:

-- The bioinformatic tool used for the present method is preferably, SMAR Scan®, which contains algorithms developed by Gene Express (~~[http://srs6.bionet.nsc.ru/srs6bin/cq_i-bin/wgetz?e-\[FEATURES-SiteID:'nR'\]](http://srs6.bionet.nsc.ru/srs6bin/cq_i-bin/wgetz?e-[FEATURES-SiteID:'nR'])~~) and based on Levitsky *et al.*, 1999. These algorithms recognise profiles, based on dinucleotides weight-matrices, to compute the 5 theoretical values for conformational and physicochemical properties of DNA. --

Please amend the paragraph starting on page 12, line 23 as follows:

--To tune the default cut-off values for the four theoretical structural criteria, experimentally validated MARs from SMART DB (~~<http://transfac.gbf.de>~~ SMART DB) were used. All the human MAR sequences from the database were retrieved and analyzed with SMAR Scan® using the "profile-like" mode with the four criteria and with no set cut-off value. This allowed the setting of each function for every position of the sequences. The distribution for each criterion was then

computed according to these data (see Fig. 1 and 3).—

Please amend the paragraph starting on page 28, line 3 as follows:

--As whole human genome sequence, all human RefSeq (National Center for Biotechnology Information, The NCBI handbook [Internet]. Bethesda (MD): National Library of Medicine (US), Oct. Chapter 17, The Reference Sequence (RefSeq) Project, 2002 (~~Available from~~ <http://www.ncbi.nih.gov/entrez/query.fcgi?db=Books>) contigs (release 5) were used and analyzed with the combined method, using SMAR Scan® as filter in the first level processing, employing default settings except for the highest bend cutoff value, whereas a stringent threshold of 4.0 degrees (instead of 3.202 degrees) has been used for the DNA bending criterion. --

Please amend the paragraph starting on page 28, line 30 as follows:

-- Table 2: Number of S/MARs predicted per chromosome. The number of genes per chromosome corresponds to the NCBI human genome statistics (Build 34 Version 3) (National Center for Biotechnology Information, The NCBI handbook [Internet]. Bethesda (NM): National Library of Medicine (US), Oct. Chapter 17, The Reference Sequence (RefSeq) Project, 2002 (~~Available from~~ <http://www.ncbi.nih.gov/entrez/query.fcgi?db=Books>) based on GenBank annotations. Chromosome sizes are the sum of the corresponding human RefSeq (National Center for Biotechnology Information, The NCBI handbook [Internet]. Bethesda (MD): National Library of Medicine (US), Oct. Chapter 17, The Reference Sequence (RefSeq) Project, 2002 (~~Available from~~ <http://www.ncbi.nih.gov/entrez/query.fcgi?db=Books>) (release 5) contig lengths. -

Please amend the paragraph starting on page 32, line 20 as follows:

--Among the three human intergenic sequences predicted to contain a "super" S/MAR using SMAR Scan® stringent settings, one of the corresponding mouse orthologous intergenic sequence is also predicted to contain a S/MAR (human EMBL ID: Z96050, position 28 010 to 76 951 orthologous to mouse EMBL ID: AC015932, positions 59 884 to 89 963). When a local alignment of these two orthologous intergenic sequences is performed, the best local alignment of these two big regions correspond to the regions predicted by SMAR Scan® to be S/MAR element. A manual search for the mouse orthologs of the two other human intergenic

sequences predicted to contain a "super" S/MAR was performed using the Ensembl Genome Browser (<http://ensembl.org>). The mouse orthologous intergenic sequences of these two human sequences were retrieved using Ensembl orthologue predictions (based on gene names), searching the orthologous mouse genes for the pairs of human genes flanking these intergenic regions.--